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(54) Title: STRUCTURE OF THE FARNESOID X RECEPTOR LIGAND BINDING DOMAIN AND METHODS OF USE THEREFOR

(57) Abstract: The present invention provides compositions comprising the ligand binding domain (LBD) of a farnesoid X receptor (FXR) in crystalline form. In alternative embodiments, the LBD of FXR is complexed with a ligand therefor. There are provided high resolution structures of FXR complexed with a novel high affinity agonist, fexaramine. The discovered structure of a FXR LBD provides the first three-dimensional view of the structural basis for FXR ligand binding. The present invention further provides a computer for producing a three-dimensional representation of FXR or a complex thereof, and a computer for determining at least a portion of the structure coordinates of FXR or a complex thereof. The present invention further provides methods of using this structural information to predict molecules capable of binding to FXR; to identify compounds with agonist, antagonist or partial agonist activity for FXR; and to determine whether a test compound is capable of binding to the LBD of FXR. The present invention further provides compositions comprising compounds identified by such invention methods.